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<120> DETOXIFIED MUTANTS OF BACTERIAL ADP-RIBOSYLATING TOXINS
AS PARENTERAL ADJUVANTS

<130> 2302-1393 / PP01393.002

<140> 09/044,696

<141> 1998-03-18

<160> 5

<170> PatentIn Ver. 2.0

<210> 1

<211> 711

<212> DNA

<213> Artificial Sequence

<220>

<221> CDS

<222> (1)..(708)

<220>

<223> Description of Artificial Sequence: wild-type Subunit
A from E. coli heat labile toxin

<400> 1

aat ggc gac aga tta tac cgt gct gac tct aga ccc cca gat gaa ata 48
Asn Gly Asp Arg Leu Tyr Arg Ala Asp Ser Arg Pro Pro Asp Glu Ile
1 5 10 15

aaa cgt ttc cgg agt ctt atg ccc aga ggt aat gag tac ttc gat aga 96
Lys Arg Phe Arg Ser Leu Met Pro Arg Gly Asn Glu Tyr Phe Asp Arg
20 25 30

gga act caa atg aat att aat ctt tat gat cac gcg aga gga aca caa 144
Gly Thr Gln Met Asn Ile Asn Leu Tyr Asp His Ala Arg Gly Thr Gln
35 40 45

acc ggc ttt gtc aga tat gat gac gga tat gtt tcc act tct ctt agt 192
Thr Gly Phe Val Arg Tyr Asp Asp Gly Tyr Val Ser Thr Ser Leu Ser
50 55 60

ttg aga agt gct cac tta gca gga cag tat ata tta tca gga tat tca 240
Leu Arg Ser Ala His Leu Ala Gly Gln Tyr Ile Leu Ser Gly Tyr Ser
65 70 75 80

ctt act ata tat atc gtt ata gca aat atg ttt aat gtt aat gat gta 288
Leu Thr Ile Tyr Ile Val Ile Ala Asn Met Phe Asn Val Asn Asp Val
85 90 95

att agc gta tac agc cct cac cca tat gaa cag gag gtt tct gcg tta 336
Ile Ser Val Tyr Ser Pro His Pro Tyr Glu Gln Glu Val Ser Ala Leu

100 105 110
 ggt gga ata cca tat tct cag ata tat gga tgg tat cgt gtt aat ttt 384
 Gly Gly Ile Pro Tyr Ser Gln Ile Tyr Gly Trp Tyr Arg Val Asn Phe
 115 120 125
 ggt gtg att gat gaa cga tta cat cgt aac agg gaa tat aga gac cgg 432
 Gly Val Ile Asp Glu Arg Leu His Arg Asn Arg Glu Tyr Arg Asp Arg
 130 135 140
 tat tac aga aat ctg aat ata gct ccg gca gag gat ggt tac aga tta 480
 Tyr Tyr Arg Asn Leu Asn Ile Ala Pro Ala Glu Asp Gly Tyr Arg Leu
 145 150 155 160
 gca ggt ttc cca ccg gat cac caa gct tgg aga gaa gaa ccc tgg att 528
 Ala Gly Phe Pro Pro Asp His Gln Ala Trp Arg Glu Glu Pro Trp Ile
 165 170 175
 cat cat gca cca caa ggt tgt gga gat tca tca aga aca atc aca ggt 576
 His His Ala Pro Gln Gly Cys Gly Asp Ser Ser Arg Thr Ile Thr Gly
 180 185 190
 gat act tgt aat gag gag acc cag aat ctg agc aca ata tat ctc agg 624
 Asp Thr Cys Asn Glu Glu Thr Gln Asn Leu Ser Thr Ile Tyr Leu Arg
 195 200 205
 gaa tat caa tca aaa gtt aag agg cag ata ttt tca gac tat cag tca 672
 Glu Tyr Gln Ser Lys Val Lys Arg Gln Ile Phe Ser Asp Tyr Gln Ser
 210 215 220
 gag gtt gac ata tat aac aga att cgg gat gaa tta tga 711
 Glu Val Asp Ile Tyr Asn Arg Ile Arg Asp Glu Leu
 225 230 235

<210> 2
 <211> 236
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: wild-type Subunit
 A from E. coli heat labile toxin

<400> 2
 Asn Gly Asp Arg Leu Tyr Arg Ala Asp Ser Arg Pro Pro Asp Glu Ile
 1 5 10 15
 Lys Arg Phe Arg Ser Leu Met Pro Arg Gly Asn Glu Tyr Phe Asp Arg
 20 25 30
 Gly Thr Gln Met Asn Ile Asn Leu Tyr Asp His Ala Arg Gly Thr Gln
 35 40 45
 Thr Gly Phe Val Arg Tyr Asp Asp Gly Tyr Val Ser Thr Ser Leu Ser
 50 55 60
 Leu Arg Ser Ala His Leu Ala Gly Gln Tyr Ile Leu Ser Gly Tyr Ser

65	70	75	80
Leu Thr Ile Tyr Ile Val Ile Ala Asn Met Phe Asn Val Asn Asp Val	85	90	95
Ile Ser Val Tyr Ser Pro His Pro Tyr Glu Gln Glu Val Ser Ala Leu	100	105	110
Gly Gly Ile Pro Tyr Ser Gln Ile Tyr Gly Trp Tyr Arg Val Asn Phe	115	120	125
Gly Val Ile Asp Glu Arg Leu His Arg Asn Arg Glu Tyr Arg Asp Arg	130	135	140
Tyr Tyr Arg Asn Leu Asn Ile Ala Pro Ala Glu Asp Gly Tyr Arg Leu	145	150	155
Ala Gly Phe Pro Pro Asp His Gln Ala Trp Arg Glu Glu Pro Trp Ile	165	170	175
His His Ala Pro Gln Gly Cys Gly Asp Ser Ser Arg Thr Ile Thr Gly	180	185	190
Asp Thr Cys Asn Glu Glu Thr Gln Asn Leu Ser Thr Ile Tyr Leu Arg	195	200	205
Glu Tyr Gln Ser Lys Val Lys Arg Gln Ile Phe Ser Asp Tyr Gln Ser	210	215	220
Glu Val Asp Ile Tyr Asn Arg Ile Arg Asp Glu Leu	225	230	235

F3
 <210> 3
 <211> 723
 <212> DNA
 <213> Artificial Sequence

<220>
 <221> CDS
 <222> (1)..(720)

<220>
 <223> Description of Artificial Sequence: wild-type CT subunit A

<400> 3		
aat gat gat aag tta tat cgg gca gat tct aga cct cct gat gaa ata		48
Asn Asp Asp Lys Leu Tyr Arg Ala Asp Ser Arg Pro Pro Asp Glu Ile		
1 5 10 15		
aag cag tca ggt ggt ctt atg cca aga gga cag agt gag tac ttt gac		96
Lys Gln Ser Gly Gly Leu Met Pro Arg Gly Gln Ser Glu Tyr Phe Asp		
20 25 30		
cga ggt act caa atg aat atc aac ctt tat gat cat gca aga gga act		144
Arg Gly Thr Gln Met Asn Ile Asn Leu Tyr Asp His Ala Arg Gly Thr		
35 40 45		

cag acg gga ttt gtt agg cac gat gat gga tat gtt tcc acc tca att	192
Gln Thr Gly Phe Val Arg His Asp Asp Gly Tyr Val Ser Thr Ser Ile	
50 55 60	
agt ttg aga agt gcc cac tta gtg ggt caa act ata ttg tct ggt cat	240
Ser Leu Arg Ser Ala His Leu Val Gly Gln Thr Ile Leu Ser Gly His	
65 70 75 80	
tct act tat tat ata tat gtt ata gcc act gca ccc aac atg ttt aac	288
Ser Thr Tyr Tyr Ile Tyr Val Ile Ala Thr Ala Pro Asn Met Phe Asn	
85 90 95	
gtt aat gat gta tta ggg gca tac agt cct cat cca gat gaa caa gaa	336
Val Asn Asp Val Leu Gly Ala Tyr Ser Pro His Pro Asp Glu Gln Glu	
100 105 110	
gtt tct gct tta ggt ggg att cca tac tcc caa ata tat gga tgg tat	384
Val Ser Ala Leu Gly Gly Ile Pro Tyr Ser Gln Ile Tyr Gly Trp Tyr	
115 120 125	
cga gtt cat ttt ggg gtg ctt gat gaa caa tta cat cgt aat agg ggc	432
Arg Val His Phe Gly Val Leu Asp Glu Gln Leu His Arg Asn Arg Gly	
130 135 140	
tac aga gat aga tat tac agt aac tta gat att gct cca gca gca gat	480
Tyr Arg Asp Arg Tyr Tyr Ser Asn Leu Asp Ile Ala Pro Ala Ala Asp	
145 150 155 160	
ggg tat gga ttg gca ggt ttc cct ccg gag cat aga gct tgg agg gaa	528
Gly Tyr Gly Leu Ala Gly Phe Pro Pro Glu His Arg Ala Trp Arg Glu	
165 170 175	
gag ccg tgg att cat cat gca ccg ccg ggt tgt ggg aat gct cca aga	576
Glu Pro Trp Ile His His Ala Pro Pro Gly Cys Gly Asn Ala Pro Arg	
180 185 190	
tca tcg atc agt aat act tgc gat gaa aaa acc caa agt cta ggt gta	624
Ser Ser Ile Ser Asn Thr Cys Asp Glu Lys Thr Gln Ser Leu Gly Val	
195 200 205	
aaa ttc ctt gac gaa tac caa tct aaa gtt aaa aga caa ata ttt tca	672
Lys Phe Leu Asp Glu Tyr Gln Ser Lys Val Lys Arg Gln Ile Phe Ser	
210 215 220	
ggc tat caa tct gat att gat aca cat aat aga att aag gat gaa tta	720
Gly Tyr Gln Ser Asp Ile Asp Thr His Asn Arg Ile Lys Asp Glu Leu	
225 230 235 240	
tga	723

F3

<210> 4
 <211> 240
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: wild-type CT

subunit A

<400> 4

Asn Asp Asp Lys Leu Tyr Arg Ala Asp Ser Arg Pro Pro Asp Glu Ile
1 5 10 15

Lys Gln Ser Gly Gly Leu Met Pro Arg Gly Gln Ser Glu Tyr Phe Asp
20 25 30

Arg Gly Thr Gln Met Asn Ile Asn Leu Tyr Asp His Ala Arg Gly Thr
35 40 45

Gln Thr Gly Phe Val Arg His Asp Asp Gly Tyr Val Ser Thr Ser Ile
50 55 60

Ser Leu Arg Ser Ala His Leu Val Gly Gln Thr Ile Leu Ser Gly His
65 70 75 80

Ser Thr Tyr Tyr Ile Tyr Val Ile Ala Thr Ala Pro Asn Met Phe Asn
85 90 95

Val Asn Asp Val Leu Gly Ala Tyr Ser Pro His Pro Asp Glu Gln Glu
100 105 110

Val Ser Ala Leu Gly Gly Ile Pro Tyr Ser Gln Ile Tyr Gly Trp Tyr
115 120 125

Arg Val His Phe Gly Val Leu Asp Glu Gln Leu His Arg Asn Arg Gly
130 135 140

Tyr Arg Asp Arg Tyr Tyr Ser Asn Leu Asp Ile Ala Pro Ala Ala Asp
145 150 155 160

Gly Tyr Gly Leu Ala Gly Phe Pro Pro Glu His Arg Ala Trp Arg Glu
165 170 175

Glu Pro Trp Ile His His Ala Pro Pro Gly Cys Gly Asn Ala Pro Arg
180 185 190

Ser Ser Ile Ser Asn Thr Cys Asp Glu Lys Thr Gln Ser Leu Gly Val
195 200 205

Lys Phe Leu Asp Glu Tyr Gln Ser Lys Val Lys Arg Gln Ile Phe Ser
210 215 220

Gly Tyr Gln Ser Asp Ile Asp Thr His Asn Arg Ile Lys Asp Glu Leu
225 230 235 240

<210> 5

<211> 240

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: wild-type Subunit
A from E. coli heat labile toxin

<400> 5
 Asn Gly Asp Arg Leu Tyr Arg Ala Asp Ser Arg Pro Pro Asp Glu Ile
 1 5 10 15
 Lys Arg Ser Gly Gly Leu Met Pro Arg Gly His Asn Glu Tyr Phe Asp
 20 25 30
 Arg Gly Thr Gln Met Asn Ile Asn Leu Tyr Asp His Ala Arg Gly Thr
 35 40 45
 Gln Thr Gly Phe Val Arg Tyr Asp Asp Gly Tyr Val Ser Thr Ser Leu
 50 55 60
 Ser Leu Arg Ser Ala His Leu Ala Gly Gln Ser Ile Leu Ser Gly Tyr
 65 70 75 80
 Ser Thr Tyr Tyr Ile Tyr Val Ile Ala Thr Ala Pro Asn Met Phe Asn
 85 90 95
 Val Asn Asp Val Leu Gly Val Tyr Ser Pro His Pro Tyr Glu Gln Glu
 100 105 110
 Val Ser Ala Leu Gly Gly Ile Pro Tyr Ser Gln Ile Tyr Gly Trp Tyr
 115 120 125
 Arg Val Asn Phe Gly Val Ile Asp Glu Arg Leu His Arg Asn Arg Glu
 130 135 140
 Tyr Arg Asp Arg Tyr Tyr Arg Asn Leu Asn Ile Ala Pro Ala Glu Asp
 145 150 155 160
 Gly Tyr Arg Leu Ala Gly Phe Pro Pro Asp His Gln Ala Trp Arg Glu
 165 170 175
 Glu Pro Trp Ile His His Ala Pro Gln Gly Cys Gly Asn Ser Ser Arg
 180 185 190
 Thr Ile Thr Gly Asp Thr Cys Asn Glu Glu Thr Gln Asn Leu Ser Thr
 195 200 205
 Ile Tyr Leu Arg Glu Tyr Gln Ser Lys Val Lys Arg Gln Ile Phe Ser
 210 215 220
 Asp Tyr Gln Ser Glu Val Asp Ile Tyr Asn Arg Ile Arg Asp Glu Leu
 225 230 235 240